37

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,719	10/09/2001	Dusan Ninkov	P06882US01	7844

22885 7590 03/23/2006

MCKEE, VOORHEES & SEASE, P.L.C.
801 GRAND AVENUE
SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,719	NINKOV, DUSAN	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-20 and 37-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-20 and 37-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment filed June 10 2005 has been received and entered. Claims 13, 15, 42 and 43 have been amended and new claims 44 and 45 have been added.

Claims 4-20 and 37-45 are pending in this application.

Rejection of claims 13, 20, 42 and 43 under 35 U.S.C. §112 2nd paragraph is no longer maintained in view of the amendment to claims 113, 15, 42 and 43.

Response to Arguments

Applicant's arguments filed June 10, 2005 have been fully considered but they are not persuasive. The rejection made in the paper mailed December 15, 2004 under 35 U.S.C. §103(a) over Ropapharm BV in view of Avery's Drug Treatment 4th edition is maintained and hereby repeated for the reasons set forth in the previous office action and those set forth below.

Previous Claim Rejections - 35 USC § 103

Claims 4-6, 8-20 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ropapharm B.V., EP 0904780A1 (Ropapharm) in view of Avery's Drug Treatment, 4th Edition, Chapter 31, pp. 1455-1509 (Avery).

Ropapharm teaches a pharmaceutical composition in the form of a solution comprising Carvacrol and/or Thymol, water, Emulgator 686 and polysorbate as being suitable for the treatment of diseases caused by *Salmonella* spp., *Pasteurella* spp., *E. coli*, *Vibrio coli*, etc. (page 2, col. 1 line 55 to col. 2, Line 5). Furthermore, the

primary reference teaches the active ingredient in the form of thymol and/or carvacrol is present in an amount of 1-10% by weight, based on the total weight of the formulation. However, the reference lacks the specific concentrations as claimed instantly in claims 14-18. Avery teaches that the dosage regimens recommended by the manufacturers of Antimicrobial drugs are purely arbitrary. The secondary reference gives guides for determining dosage amounts, but says that values will depend on the health, age, and pharmacokinetic characteristics of the patient. (Page 1489, col. 1, 4). Dosages of Antimicrobial Drugs - col. 2, 4.1 Dosages at Extremes of Age. Moreover, while the references are silent regarding the specific percentages by weight of thymol and carvacrol as claimed instantly, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. As anyone of ordinary skill in the art will appreciate, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find *workable* conditions generally involves no more than the application of routine skill in the art of chemical engineering. See, only as exemplary, the dicta of *In re Aller* 105 USPQ 233. Similarly, the determination of *optimal* values within a disclosed range is generally considered obvious. See, only as exemplary, the dicta of *In re Boesch* 205 USPQ 215.

For these and other self-evident reasons, it would have been obvious to one having ordinary skill in the art at the time the inventions was made to have modified the composition of Ropapharm comprising thymol and carvacrol by adjusting the concentrations of the antimicrobial drugs as suggested by Avery because of the

reasonable expectation of obtaining a composition comprising a mixture of thymol and carvacrol which would be capable of treating diseases caused by bacterial infections.

Claims 4-9, 12-20 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ropapharm B.V. EP 0904780A1 and further in view of Remington's Pharmaceutical Sciences, 15th Edition, 1975, pages 1405-1412.

Determining the scope and contents of the prior art

Ropapharm teaches a pharmaceutical composition in the form of a solution comprising Carvacrol (isopropyl o-cresol) and or Thymol (applicants refer to Thymol as isopropyl-cresol), water, Emulgator 686 and polysorbate (page 3, column 1, line 50 to column 2, line 17). The reference teaches the pharmaceutical compositions as being suitable for the treatment of diseases caused by *Salmonella* spp., *Pasteurella* spp., *E. coli*, *Vibrio coli*, etc. (page 2, column 1, line 55 to column 2, line 5). The reference teaches the active ingredient in the form of thymol and/or carvacrol is present in an amount of from 1 to 10% by weight based on the total weight of the formulation (page 2, column 2, lines 49-56) for treatment of poultry, including turkeys, as in instant claim 19 and the use as an injectable composition comprising both thymol and carvacrol in amounts which overlap those claimed in instant claims 8-9 and 12, for the treatment of diseases caused by infections of instant claim 20.

Ascertaining the differences between the prior art and the claims at issue

The primary reference lacks the sodium chloride of instant claim 13 and 42. Remington teaches that knowledge of colligative properties of solutions is essential for one to understand fully the principles involved in rendering intravenous solutions

isotonic with blood serum. To produce less shock and less irritation than those which are hypotonic or hypertonic, and present-day practice recognizes the desirability of making the necessary adjustment whenever possible. Finally, the secondary reference teaches that the usual practice is to add wither sodium chloride or dextrose to adjust hypotonic intravenous solutions to isotonicity (page 1405, column 1, line 1 to page 1406, column 1, line 34).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the isotonicity of the injectable formulation of Ropapharm by adjusting the tonicity of the solution using sodium chloride, the salt which is usually used for adjusting tonicity of injectable solutions because of the reasonable expectation that sodium chloride would adjust the formulation to produce less shock and less irritation.

Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ropapharm B.V., EP 0904780A1 (Ropapharm) and further in view of Remington's Pharmaceutical Sciences, Fifteenth Edition, 1975, pp.1405-1412 as applied to claims 4-9, 12-20 and 37-43 above, taken together with The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals 12th Edition, 1996 page 9539 (Merck) and common knowledge in the art.

The combined references above teach a solution comprising Carvacrol (isopropyl o-cresol) and/or Thymol (isopropyl-cresol), water, Emulgator 686 and polysorbate, which is adjusted for isotonicity using either sodium chloride or dextrose, however, the combined references lack the specific oils of claims 10-11.

The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition, 1996, page 9539 (Merck).

Merck teaches 1 gram of Thymol dissolves in 1.7 ml olive oil at 25 degrees. Since this is a claim to a composition, and the intended use of said composition is not given patentable weight unless it results in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since Merck teaches the specifically claimed antimicrobial compound in the specifically claimed pharmaceutically acceptable carrier, it meets the limitations of instant claims 11. It is common knowledge that vegetable oil is a cheap, easily obtained alternative to olive oil.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the solution comprising Carvacrol (isopropyl o-cresol) and/or Thymol (isopropyl-cresol), water, Emulgator 686 and polysorbate, which is adjusted for isotonicity using either sodium chloride or dextrose, by adding olive oil as suggested by Merck, or by using a cheaper, easily obtained vegetable oil, because of the reasonable expectation of obtaining an injectable pharmaceutical composition, comprising a readily available pharmaceutically acceptable carrier, which has the desirable property of solubilizing thymol.

Applicant asserts that a prima facie case of obviousness has not been made because Claim 5 recites a composition comprising (a) at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base; and (b) a pharmaceutically acceptable carrier for parenteral

administration. Applicant asserts that the term "reacting" refers to a process in which the organic phenolic compound is chemically modified which involves the deprotonation of the alcohol moiety to form an aryl oxide anion which then associates with the Group I cation in solution. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the chemical modification of the organic phenolic compound, particularly the deprotonation of the organic phenolic compound, which then associates with the Group I cation from the Group I salt) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Secondly, absent unexpected results, it would be reasonable to expect that a pharmaceutical composition comprising Carvacrol (isopropyl-o-cresol) and/or Thymol (isopropyl cresol) when adjusted for isotonicity using sodium chloride as taught by Remington's Pharmaceutical Sciences, would react with one another because of the species would be solvated in solution.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-20 and 37-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 20-23 of U.S. Patent No. 6,414,036. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to pharmaceutical compositions comprising the same ingredients for the same purpose. The instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires the particular organic phenolic compound, chemically reacted with a Group I salt and further conflicting claims recite the particular sodium chloride reacted with isopropyl-o-cresol and isopropyl-cresol. None of the instant claims recites that specific weight percentage and it does not recite the parenteral administration. One skilled in the art would have been motivated to prepare additional useful compositions of the ranges taught by the prior art. While the reference is silent regarding some % concentrations, the difference in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. When the

general conditions are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 45, 105 USPQ 233, 235 (CCPA 1955). In the absence of any criticality and/or unexpected results of the additional ranges claimed, the instant invention is considered obvious. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970). This rejection is repeated from the office action dated July 3, 2003.

Claims 4-20 and 37-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,844,369. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to pharmaceutical compositions comprising the same ingredients. The instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires carvacrol and thymol, in combination with a transition metal generally. Claim 6 further requires hydroxide. None of the instant claims recites the purpose of a pesticidal composition. It is noted that the reference does not teach that the composition can be used in the manner instantly claimed, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference

composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. Further, "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Some of the claimed percentages differ; however, one skilled in the art would have been motivated to prepare additional useful compositions of the ranges taught by the prior art. While the reference is silent regarding some % concentrations, the difference in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. When the general conditions are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 45, 105 USPQ 233, 235 (CCPA 1955). In the absence of any criticality and/or unexpected results of the additional ranges claimed, the instant invention is considered obvious. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Claims 4-20 and 37-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,649,660. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to pharmaceutical compositions comprising the same ingredients for the same purpose. The instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires the particular antimicrobial compound selected from sodium isopropyl-o-cresol, sodium isopropyl-cresol, potassium isopropyl-o-cresol and potassium isopropyl-cresol. None of the instant claims recites that specific weight percentage, however, the instant claims overlap and encompass the conflicting claims. It differs in that it does not recite parenteral administration. One skilled in the art would have been motivated to prepare additional useful compositions of the ranges taught by the prior art. While the reference is silent regarding some % concentrations, the difference in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. When the general conditions are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 45, 105 USPQ 233, 235 (CCPA 1955). In the absence of any criticality and/or unexpected results of the additional ranges claimed, the instant invention is considered obvious. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as

broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Donna Jagoe
Patent Examiner
Art Unit 1614

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

BRUCE KISLIUK, DIRECTOR
TECHNOLOGY CENTER 1600

March 16, 2006